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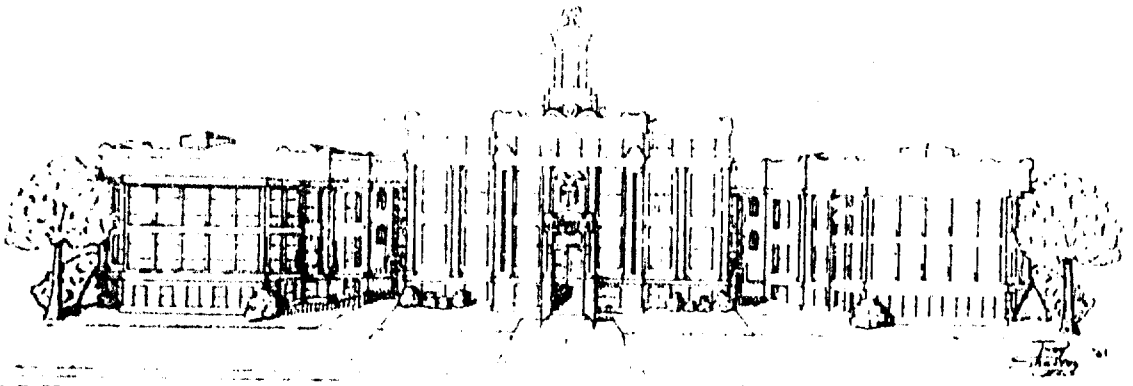

ALPHA-1 GLOBULINS IN THOSE SUSCEPTIBLE TO VIRAL ACUTE RESPIRATORY DISEASES

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ALPHA-1 GLOBULINS IN THOSE SUSCEPTIBLE TO VIRAL ACUTE RESPIRATORY DISEASES

By

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A high frequency of elevated initial serum alpha-1 globulin levels was noted among naval recruits who subsequently appeared to be more susceptible to acute viral respiratory diseases.

Correlating the biological indices with host resistance in disease patterns presents a real challenge. Qualitative and quantitative differences in susceptibility to infection also needs to be evaluated (1-3). During epidemiological surveys, individual differences were seen in which 50-60% of the recruits had an average of more than two discrete respiratory episodes, while 10-20% remained disease-free throughout the same training period (4). The study of the host is therefore of significant importance, since other extensive studies have failed to show why some recruits are more susceptible to respiratory infection than others (3-5).

The purpose of this paper is to determine the value of the initial serum alpha-1 globulin moiety in predicting susceptibility to respiratory infection.

MATERIALS AND METHODS

Population:

The study population consisted of two companies of recruits in basic training at the Great Lakes Naval Training Center. One company (A, 55 men) underwent training from November 1959 through January 1960. The other (B, 69 men) trained from July through September 1960. Recruits at this training center are predominantly 17-19-year olds from the eastern half of the United States.

Sampling procedures:

The men in both companies were first observed within 24-48 hours after their arrival, and were subsequently interviewed (MJM) at 0700 on Mondays, Wednesdays and Fridays, when oral temperatures and symptoms of respiratory disease were recorded. The

presence or absence of symptoms on non-interview days was also recorded.

A discrete respiratory disease episode was considered to have occurred if the symptoms of an individual differed in intensity, quality, or number from his usual pattern, and were present for at least two days. A patient with respiratory infection was considered febrile if the oral temperature was 100°F or above (2).

Collection of specimens:

At least three specimens were collected from every recruit who was observed for the entire training period, i.e., one within two days of his arrival, one during the middle (approximately 4th week) and, one just before completion of training. Specimens were also obtained at the onset of acute respiratory disease and three weeks convalescent. All were stored at -20°C until tested.

Laboratory procedures:

Serologic tests:

The following antigens were used in the complement fixation (CF) tests: influenza viruses - type A strain (A2/Japan/305/57) and type B strain (B/GL/1760/54). Parainfluenza viruses-types 1 (HA-2) and 3(HA-1)*. Adenovirus - types 3, 4, and 7 grown in HeLa cell cultures in this laboratory. Tests were performed by the modified Kolmer technique using two full units of complement and antigen (6).

Paper strip electrophoresis:

Serum protein distributions were determined on each recruit without knowledge of their respiratory disease pattern. Six lambda (.006 ml) of serum was applied at the center of 3X30.5 cm strip of Whatman No. 1 filter paper in a Durrum type cell. Specimens were

*Microbiological Associates

allowed to resolve for 16 hours in a barbital buffer system (pH 8.6 at ionic strength .05 M) in a current of .1 ma (width of strip). Strips were then fixed and stained with bromphenol blue in accordance with procedures outlined elsewhere (7, 8). Serum protein distributions were measured with the Spinco model R analytrol.

RESULTS

The results in Table 1 indicate that the average number of discrete respiratory episodes in the two companies of recruits was remarkably similar, therefore, no attempt has been made to present these data in reference to individual companies.

The distribution of serological antibody responses among the 119 recruits is presented in Table 2. One of the most striking observations to be made from these data is that very few (15.6%) failed to respond to at least one of the battery of antigens tested, while over 50% revealed significant antibody responses to 2 or more viral antigens.

The distribution of respiratory episodes and serological antibody rises in naval recruits is illustrated in Figure 1. Respiratory disease episodes (representing acquisition of new agents) were concentrated in the first 4 weeks of training with distinctive disease peaks at 10 and 25 days (Fig. 2). The serological antibody responses were also of a bimodal nature with an interval of 15 days between peaks which followed the respective episodes by 10 days. An additional flare-up was evident near the end of the recruit training period (60-65 days).

Figure 3 shows a comparison of the initial alpha-1 globulin levels of each individual with their subsequent number of respiratory episodes. Significantly elevated values (3.5 mg%) were found at a greater frequency among recruits who subsequently experienced more than 2 discrete episodes (see also lower half of Table 3). A more detailed investigation of recruits who experienced either single or multiple antibody responses is graphically compared to their alpha-1 globulin levels in Figure 4 --- difference being apparent not only within, but between groups

selected for single or multiple response. Initial serum alpha-1 globulin levels were not found to be significantly elevated in recruits who subsequently developed only antibody responses to either HA-1 or 1760 or to both. Evidence of antibody response to J-305, either alone or in combination with other antigens, was most commonly seen in recruits with significantly elevated alpha-1 globulin levels in their initial or subsequent serum specimens. A positive correlation, as shown in Figure 5, resulted from a comparison of the percentage of significantly elevated alpha-1 globulin with the number of antibody responses.

In Table 3 the mean alpha-1 globulin values and antibody responses are compared with the number of clinical episodes. In those men who had three or more respiratory episodes, initial alpha-1 globulin levels higher than 3.5 mg% are significantly more frequent ($p = <0.001$).

DISCUSSION

The frequency of discrete respiratory episodes among the military population described indicated that very few recruits completed training without experiencing a respiratory infection. In fact, an average of more than 2 discrete upper respiratory infections per man occurred during the Fall-Winter and Summer study period. A high incidence of viral respiratory infections was also indicated by the serological data. Over 50% of the men acquired responses to more than one respiratory antigen. Seventy-five percent of the individuals who experienced more than 2 different respiratory infections had significantly elevated initial serum alpha-1 globulin values. These results might have been even more significant if the nature of antibody response to influenza 1760 were known. An antibody response to influenza 1760 without clinical symptoms, and isolations during the across-the-board influenza vaccine program (although these companies were exempt) may indicate that antibody rises resulted from immunization. If so, then significantly elevated alpha-1 globulin levels might be used as an index in predicting susceptibility to natural respiratory diseases, as compared with those resulting from a vaccine response. To evaluate this, a knowledge of the role of

this parameter in antibody responses would be extremely important. Clinical symptoms, serological response and normal alpha-1 globulin levels may well indicate a difference in responsiveness to immunization rather than a natural episode. Statistically significant differences were found in both the epidemiological and serological response groups with respect to their alpha-1 globulin levels.

SUMMARY

The respiratory disease pattern observed in two companies of naval recruits during a 1959-1960 (Fall-Winter and Summer) epidemiological survey, indicated an average of more than 2 discrete respiratory episodes per man. Over 50% demonstrated antibody responses to multiple antigens, while only 15.6% failed to show a serological rise to a viral respiratory antigen. Most of the new infections were acquired during the first half of the training period. There were two distinct peaks of clinical disease. The first occurred on the 10th day of training and the second on the 25th day. The peaks of clinical disease were followed in both instances by serological peaks 10 days later.

The alpha-1 globulin values were found to be significantly elevated in 40% of the recruits who subsequently demonstrated multiple serological responses. Seventy-five percent of the recruits considered to be susceptibles on the basis of demonstrating more than 2 discrete respiratory episodes had significantly elevated initial serum alpha-1 globulin levels. A highly significant relationship ($p = <0.001$) was found between number of discrete episodes and the alpha-1 globulin levels.

TABLE I

Respiratory Disease in Two Companies of Naval Recruits during Nine Weeks of Training in the Winter of 1959-60 (Company A) and the Summer of 1960 (Company B)

Companies	Population	Total ARD*	Average number ARD per man
A	50	117	2.3
B	69	151	2.2

*Acute respiratory disease

TABLE 2

The Distribution of Significant Serological Antibody Responses to Seven Selected Acute Respiratory Viral Agents among Naval Recruits during the 1959-1960 Epidemiological Study

Serological responses - 119 recruits

Number of antigens	Percent recruits developing antibody rises
0	15.6
1	31.2
2	34.4
3	12.8
4	6.2

TABLE 3

Relationship of the Mean Alpha-1 Globulin among the Initial Serum Specimens with the Antibody Responses and the Number of Discrete Episodes

	Number of episodes*				
	0	1	2	3	4
Mean					
Alpha-1 globulin (mg%)	2.3	2.24	2.46	3.9**	4.25**
Antibody response (No. of antigens)	0	1.1	1.8	1.7	2.33

	Number of serological rises†			
	0	1	2	3
Mean				
Alpha-1 globulin	2.28	2.79	3.56**	3.71**
Episodes	.83	2.1	2.55	3.0

*F 21.55 p = <0.001 significant difference between groups (episodes)

**Significantly elevated (3.5 mg%)

† F 5.17 p = <0.01 significant difference between groups (serological)

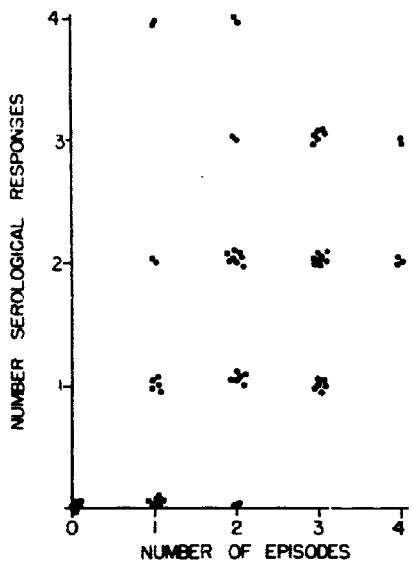

FIG. 1 Disease episodes and significant rises to selected respiratory viruses.

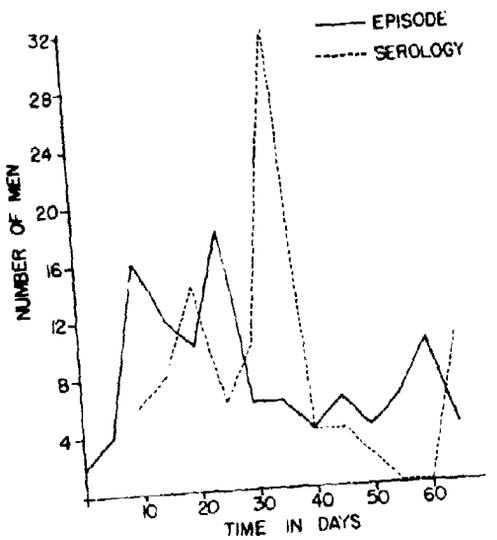

FIG. 2. Comparison of significant antibody response with that of respiratory episodes. Time in days relationship of respiratory episodes and development of viral antibodies.

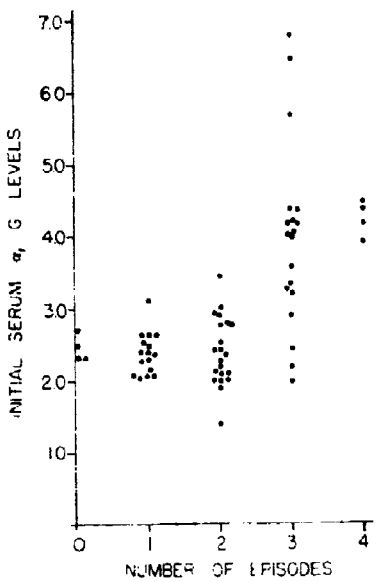

FIG. 3. Initial serum alpha-1 globulin levels as related to respiratory episodes during the recruit training period.

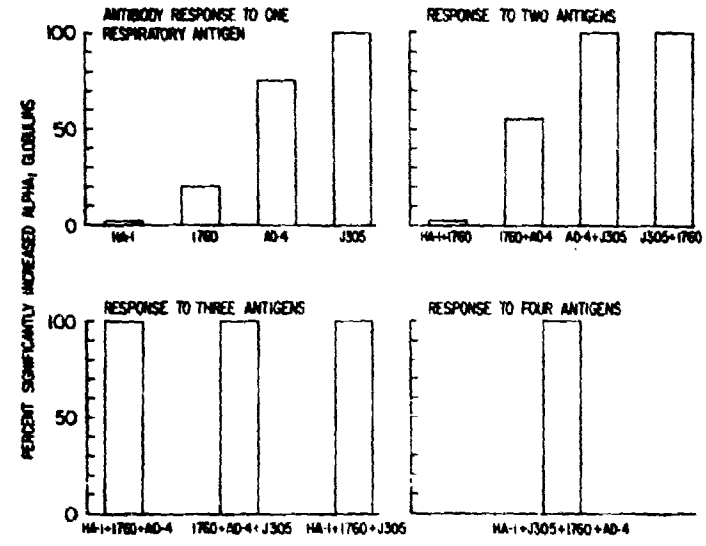

FIG. 4. Percent of significantly increased alpha-1 globulins (above 3.5 mg%) among recruits who subsequently demonstrated either single or multiple antibody responses

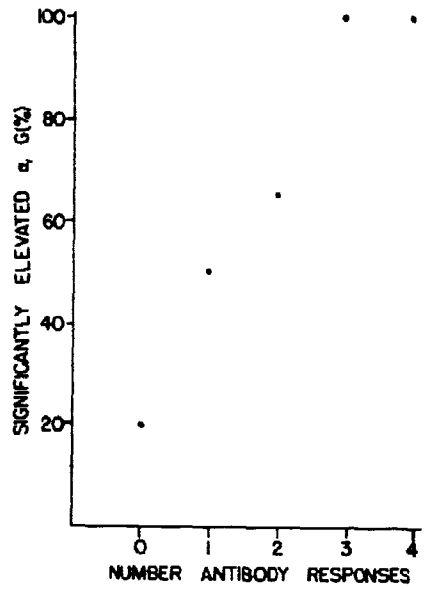

FIG. 5. Positive correlation of antibody response with percent recruits having significantly elevated alpha-1 globulins.

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13 ABSTRACT

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